Chapter 2 Low Molecular Weight Gelators

In this chapter the field of low molecular weight gelators (LMWGs) is reviewed. Several systems based on differing self-assembly processes are discussed. The emphasis in this chapter is placed on the various techniques used to characterise the properties of organogelators in the gel state and to determine the contribution and effect of intermolecular interactions on these properties.

This chapter concludes with a discussion of the "second" generation of gelators, which rather then being discovered through serendipity, where designed to gelate through guided intermolecular interactions to provide optimal anisotropy. The application of LMWGs is discussed, briefly, together with challenges facing the field.

2.1 Definition of a Gel

In daily life most people encounter systems based on gelating agents, often without realising it. From a scientific perspective a definitive definition of a gel is still lacking, mainly due to the chemical diversity encountered in gelation science. The gel state has been recognised already for over 150 years. In 1861 Thomas Graham gave the following description: *while the rigidity of the crystalline structure shuts out external expressions, the softness of the gelatinous colloid partakes of fluidity and enables the colloid to become a medium for liquid diffusion, like water itself*.[1] In the following years scientists attempted to define the "gel" state in a more explicit manner. Dorothy Jordon Lloyd proposed in 1926: the colloid condition, the "gel" is one which is easier to recognise than to define and postulated: *only one rule seems to hold for all gels and that is that they must be built up from two components, one which is a liquid at the temperature under consideration and the other which, the gelling substance proper, often spoken of as the gelator, is a solid. The gel itself has the mechanical properties of a solid, i.e. it can maintain its form under stress of its own weight and under any mechanical stress it shows the phenomenon of strain*.[2]
In the following years more rigorous definitions were proposed which attempted to link the microscopic and macroscopic properties of a gel.[3,4] Based on these definitions a substance is a gel if it (1) has a continuous microscopic structure with macroscopic dimensions that is permanent on the time scale of analytical experiments and (2) is solid-like in its rheological behaviour despite being mostly liquid.[5] Nevertheless, for screening programmes the succinct definition of Jordon Lloyd is still useful: *if it looks like a gel it must be a gel*.[2]

In general, a gel is the result of the self-assembly process of compounds which are capable of forming a 3D-network. Due to the formation of this network the solvent is not able to flow and the solvent, which is liquid at high temperatures, is solidified at room temperature.
Gels can de divided in two separate classes, chemical and physical gels. The chemical gels are classified as gels in which the aggregation is driven by the formation of covalent cross-links between the compounds and this aggregation leads to the formation of a thermally irreversible network.[6] Examples of these systems include cross-linked polymeric systems,[7] which can be used for triggered drug release[8,9] or inorganic oxides.[10] Physical gels systems are formed by non-covalent interactions and, hence, the gel formation is thermally reversible, which makes this type of gelators an excellent subject for studies into supra-molecular chemistry.

In this chapter only physical gels will be discussed and as several recent reviews cover physical gelators already[5,11,12] this chapter will not try to be comprehensive, but rather it will focus on the properties of the structures necessary to achieve gelation and discusses the various techniques employed in studying and understanding gelation behaviour.

Compounds able to form physical gels include clays,[13] polymers, proteins, colloids and certain small organic compounds. Compounds of this latter group are called low molecular weight gelators (LMWGs). LMWGs are gelators consisting of organic compounds with a molecular weight of less then 2000 Da which show gelation behaviour in organic solvents and sometimes in water. Due to the special chemical nature of liquid water compared to organic solvents,[14,15] compounds able to gelate water are sub-classified as hydrogelators. Again, several recent reviews focussing on hydrogelators have been published.[16,17] In this thesis LMWGs are described which gelate only organic solvents and therefore this chapter will focus primarily on these types of gelators.

2.2 Gels based on Various Types of Intermolecular Interactions

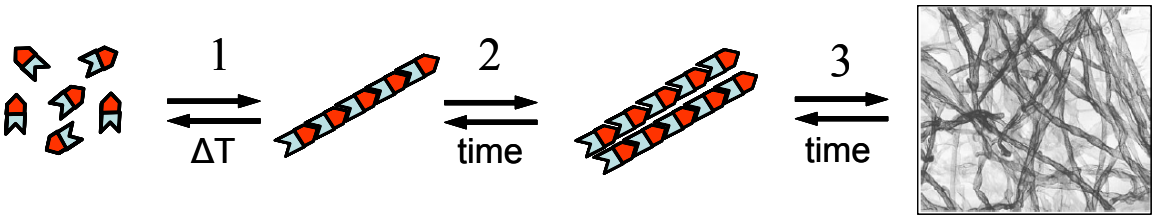


Figure 2-1. Schematic representation of the formation of a 3D- network starting form dissolved gelator molecules.

The formation of a gel occurs, in general, via the following steps (Figure 2-1). At elevated temperatures the gelator molecules are dissolved completely. These temperatures are required to overcome the driving force for aggregation due to strong intermolecular interactions. Upon cooling of the solution these intermolecular interactions provide the driving force for the molecules to self-assemble (1). Due to an anisotropy in these interactions self-assembly is favoured in one dimension and leads to the formation of thin fibers. Along the fibers new fibers can grow or assemble, thereby creating bundles consisting of several thin fibers which minimises the large surface free energy of the single fibers (2). Over time these bundles grow and can occasionally split leading ultimately to the formation of a 3D-network (3). This is recognised at the macroscopic level as the formation of a gel.

It has been demonstrated that anisotropy in intermolecular interactions leading to self-assembly of gelator molecules is necessary for the formation of a gel fiber.[11,18] Intermolecular interactions between gelator molecules can include London dispersion forces, ionic-ionic, dipole-dipole, hydrogen bonding, van der Waals and π-π stacking interactions and in the majority of gel systems reported the combination of these forces are responsible for gelation. It has been demonstrated that there is a delicate balance between gelator structure, intermolecular interactions and gelation properties. A small change in the molecular structure of the gelator can change the molecule from a gelator into a non-gelator.[19] When the molecules still aggregate, the result is crystallisation instead of gelation,[20] or aggregation can be completely absent and the compound is soluble.[21]
Gels are formed under kinetic control and due to presence of long gel fibers there is a large surface free energy, which makes the gel state a meta-stable state.[22] The thermodynamically most stable state is the crystalline state and it is apparent from studies that there must be a anisotropic driving force in the aggregation that inhibits crystallisation and leads to the formation of a gel instead.[11] It was found that flexible or branched alkyl chains can hinder crystallisation, although it remains difficult to prevent crystallisation altogether.[23]

There are many compounds, which can form gels due to various types of intermolecular interactions and a large structural diversity exist between these molecules (Figure 2-2).

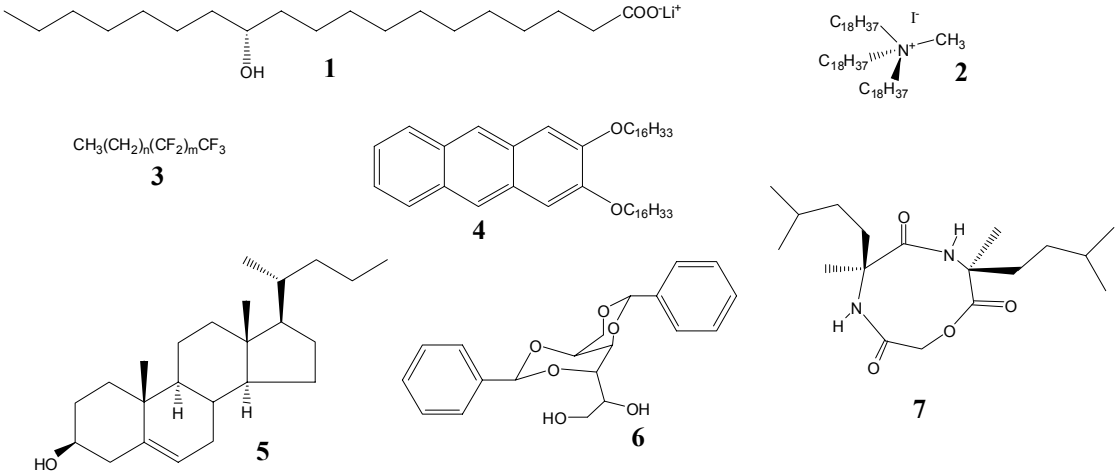


Figure 2-2. Structure of various low molecular weight gelators.

Amongst the oldest of gelators known are metallic soaps, which are used in cosmetic applications. An example of a metallic soap gelator is the lithium salt of 3-hydroxy stearic acid **1**.[24] This gelator aggregates via several intermolecular interactions: ionic interactions between the metal ions, van der Waals interactions between the alkyl tails and hydrogen bonding interactions between hydroxyl groups.[25] Cationic surfactants are related structurally to the metallic soaps. Quaternary ammonium salts with long alkyl chains, *e.g.* **2** show gelation behaviour due to aggregation driven by Coulombic and solvophobic interactions.[26] Gelators which function through solvophobic effects include perfluorinated compounds, *e.g.* **3** in aliphatic hydrocarbons. Due to their immiscibility with the solution phase at room temperature these compounds form a separate phase, which leads to gelation.[27] Molecules in which the intermolecular interactions are based on π-π and van der Waals interactions consist of functionalised aromatic systems, *e.g.* bis(alkyloxy)anthracene **4**, which form gels in aliphatic solvents.[20]

These are examples of gelators, which are relatively simple in structure. However, more complex compounds display gelation behaviour also and are often based on natural products. Certain steroids, *e.g.* cholesterol **5**, are able to gelate hydrocarbons.[28] The ability of these compounds to aggregate is related to their molecular rigidity and the aggregation properties of the steroid skeleton and gelation for this type of compound is driven by van der Waals interactions. Derivatives of sugars are know to display gelation behaviour also, *e.g.* dibenzylidene-D-sorbitol (DBS) **6**, which is an efficient gelator for both organic solvents and water. Its gelation behaviour has been known since 1942.[29] This compound self-assembles *via* π-π and hydrogen bonding interactions that create stable gel fibers in organic solvents as well as in water.
Peptide-based structures are also known to display gelation behaviour, *e.g.* depsipeptide **7** forms gels in various organic solvents.[30] In this type of system the gelation behaviour is based on hydrogen bonding interactions. The structure of the molecule can be even more complex, such as vancomycin which, when modified with pyrene, is reported to act as a gelator.[31]

2.3 Characterisation of Properties of Gel Fibers

The gelators systems discussed above have been known for over 15 years. However, due to the large structural diversity of these systems the physiochemical basis for their gelation behaviour has taken a considerable time to be established. Many different techniques have been used or were developed to study the properties of gels. These techniques are used to determine which intermolecular interactions are involved in self-assembly leading to gelation, or to establish the morphology of the gel and gel fibers, or determine the thermotropic and viscoelastic properties.

The goal using these techniques is to gain insight into the relationship between the structure of the gelators and the properties of the gel. Ultimately, the aim is to predict the gelation behaviour of new compounds prior to their synthesis and to be able to design gelator molecules for specific solvents.

2.3.1 Phase Diagrams

All low molecular weight gelators require a minimum of material in order to be able to form a gel as there has to be sufficient material present for the formation of a 3D network. Additionally, all compounds are soluble to a certain extent in a solvent. The amount of a compound necessary for gel formation is called the critical gelation concentration, cgc. This value consists of two components: the concentration of gelator in the solvent, C_{sol}, and the concentration of aggregated gelator, C_{agg} (Figure 2-3).

Gel fibers are formed via non-covalent interactions and these aggregates become less stable at elevated temperatures, at which the solubility of the compound is increased. The temperature at which the gel looses it structural integrity is called the gel-sol phase transition or T_{gs}. The temperature at which this occurs depends on the structure of the gelator, the nature of the solvent and the concentration. The T_{gs} can be determined by various visual inspection techniques, *e.g.* by the "dropping ball" technique,[32] bubble motion[33] or the inverted test tube method.[34]

In a dropping ball measurement a small steel ball is placed on top of the gel and the gels are heated slowly while the position of the ball is monitored. At the T_{gs} the gels are no longer able to withstand the weight of the ball and the ball drops to the bottom of the vial. In the bubble movement experiment, bubbles can be either injected in the sample or may remain in the sample after preparation. The sample is heated slowly while the position of the bubble is monitored. When the bubble moves through the sample with the same speed compared to the liquid, the T_{gs} has been reached. In the inverse test tube method the sample is heated and the test tube is inverted occasionally. When the sample flows under its own weight, the T_{gs} is considered to be reached.

By determining the T_{gs} in a solvent over a range of concentrations the phase diagram of that gelator can be drawn. For most of the gelators it is found that there is an exponential increase of C with T_{gs} (Figure 2-3).

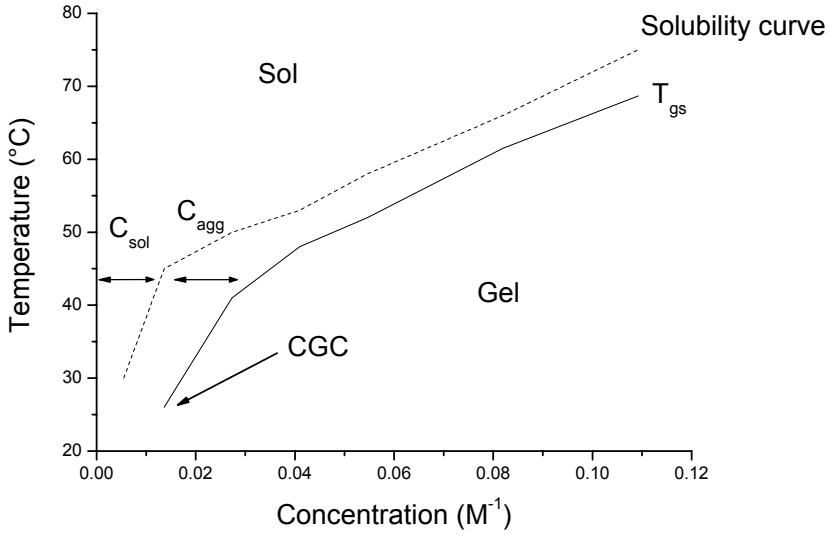


Figure 2-3. Example of a phase diagram for a gelator in a solvent.

The drawback of these methods is that they only measure the gel-sol transition temperature and not the solubility of the gelator. The T_{gs} corresponds only to the temperature at which the gel looses its structural integrity and some of the compound may be aggregated still, however these aggregates are too small to sustain a network.

2.3.2 Calorimetry of the Gel-Sol Transition

There are two methods which are employed frequently to determine the strength or enthalpy (ΔH_g) of the intermolecular interactions in the gel.
In the first method it is assumed that the gel-sol transition can be interpreted as dissolution of crystals in ideal solutions and, therefore, via the van't Hoff equation[35,36] (Equation 2.1) the melting enthalpy of the gel can be determined.

$$\frac{d \ln (C)}{d (1/T_{gs})} = - \frac{\Delta H_g}{R}$$

Equation 2.1

This method is based on the logarithmic relationship between concentration and T_{gs}. However, as the T_{gs} usually corresponds to the temperature at which the gel network breaks down and as a significant part of gelators are aggregated still, the value used for C in this equation is often too high. As a consequence the values obtained for ΔH_g via this method are usually too low.

A more direct method to determine the melting enthalpy involves Differential Scanning Calorimetry (DSC). In this technique a sample cell and reference cell are maintained at the same temperature and the power consumption required to heat the sample over a temperature range is measured. The difference in heat flow between the sample and reference cell is related to a change in the physical state of the sample, *e.g.* it melts, dissolves, etc. When this technique is applied for gels the energy required for the dissolution of the gel fiber is measured and ΔH_g can be determined directly.[37] As the first method leads to an undrestimation of ΔH_g, the values for H_g obtained by DSC are often more reliable.

2.3.3 Gel Fiber Morphology

There are several methods employed to determine fiber morphology. These methods include direct imaging techniques such as Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM). In TEM and SEM experiments a gel patch is dried and, often, stained with a heavy element to enhance the contrast. After that, the samples are placed in an ultra-high vacuum and imaged with an electron beam. In these methods the gel fibers are not imaged in their native state and artefacts may arise upon drying and staining as this will induce stress in the gel fiber.

An indirect method used to determine fiber morphology is based on scattering techniques *i.e.* Small Angle X-ray Scattering (SAXS) or Small Angle Neutron Scattering (SANS) in which the sample is hit by a beam of X-ray or neutron radiation.[38,39] The particles in the beam are scattered depending on the shape of the fibers and via mathematical treatment of the scattering intensity as a function of the angle, the size and morphology of the gel fibers can be determined.[40] The problem with this method is that some knowledge of the size and shape of the gel fibers is required to perform the mathematical treatment. Also, if the sample is not homogeneous the mathematical treatment becomes difficult.[5] However, as the gels are imaged in their natural environment these methods provide invaluable information.

2.3.4 Viscoelastic Properties of a Gel

Rheology deals with the deformation and flow of matter under the influence of stress. These properties are measured by a rheometer, in which the compound is placed in the sample holder in which it is subjected to shear. The viscoelastic properties of the compound are determined as terms of the viscoelastic storage G' and loss moduli G''.[41] These values are obtained from oscillatory rheology experiments and G' represents the amount of energy that can be stored in the sample and indicates the elasticity of the sample. G'' is derived from the amount of energy absorbed by the sample which is related to the energy lost in the sample by non-elasticity.

Gels can behave either as viscoelastic liquids or as viscoelastic solids, which is due to the formation of a highly dynamic or a static network structure, respectively. Two types of rheological measurements often performed on gels are the determination of the mechanical stress resistance and the dynamic moduli.

In general, the dynamic moduli depends on the frequency (time scale) of the measurement. The observed frequency dependence gives insight into the relaxation and lifetime of the bonds between the gelator molecules.[42] If the bonds have a permanent character, only a small frequency dependence is expected and G'>>G'' at all frequencies. This is often found for static network structures. Examples of these systems are gel networks formed by benzohydroxamic acid derivatives[43] or bisurea gelators.[44]

If the bonds have a temporary character, a significant frequency dependence is observed, with G'< G'' at low frequencies and G'> G'' at high frequencies. This is observed for wormlike micelles.[45,46]

The amount of mechanical stress that gel network can resist, is determined by measurement of the linear regime of the dynamic moduli as a function of stress amplitude, *i.e.* the regime where G' and G'' are independent of the stress amplitude. At a certain level of stress, the gel network is not able to withstand the stress applied and a sharp decrease of G' is observed. The stress value at which this occurs is considered the maximum stress a network can resist.

2.3.5 Organisation in the Gel Fiber

The organisation of the molecules in a gel fiber is one of the most relevant questions in the study of gelling agents. When the organisation in the gel fiber is known it provides direct information on the different intermolecular interactions present in the gel fiber and how these contribute to the gel properties. 2D NMR spectroscopy and single crystal X-ray diffraction are applied normally to determine the organisation in supra-molecular structures. However, 2D NMR spectroscopy is of limited use as the gel fibers are in the solid state and do not give a clear signal.[47] Single crystal X-ray diffraction can be performed only on crystals of sufficient size and the gel state makes it difficult to obtain crystals suitable for diffraction. Only in a few instances has the crystal structure of a gelator been resolved.[48,49] Also, the question still remains if the crystal structure obtained from the gelator in the crystalline state corresponds to the organisation in the gel fiber.

Therefore, Powder X-ray Diffraction (XRD) is used, which provides information of the organisation of the gel fiber. By this technique simple phases such as lamellar and hexagonal phases can be determined easily from the Bragg diffraction pattern.[50] When the XRD patterns of the crystalline and gel state are comparable, it is concluded that their organisation is similar. However, it has not been possible yet to determine a fiber structure by this technique alone.

By FTIR and Raman spectroscopy information on the organisation is obtained in an indirect manner. From the position of the vibrations in the spectra the chemical environment of the different functional groups in the molecules are probed. By comparison of dissolved gelators with gelators in the gel state, the specific intermolecular interactions leading to gel formation can be deduced. A significant advantage of these techniques is that these can be applied to the native state of the gel.

2.4 Rational Design of Gelators

From the studies of the many gelators reported so far it is known that anisotropy in the intermolecular interactions is a prerequisite for gel formation and uni-dimensional gel fiber growth.[11,18] With this design principle in hand many systems have been developed over the years to maximize the anisotropy of the intermolecular interactions in order to make successful gelling agents. The anisotropy can be guided via hydrogen bonding interacting by moieties which possess this property, *e.g.* amides, ureas and urethanes.[51] These groups have shown to be successful design motifs for gelators due to their inherent strength, self-complementarity and directionality and in this perspective many new types of organogelators have been developed.

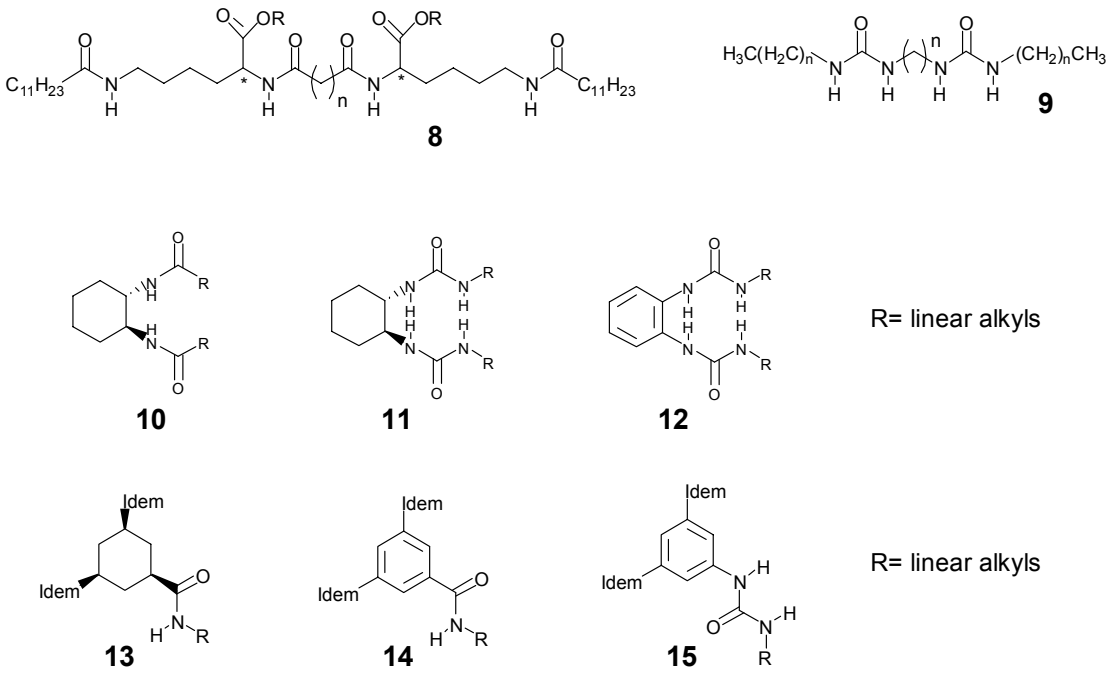


Figure 2-4. A selection of gelators based on different types of hydrogen bonding interaction.

Amide and urea groups are used frequently to introduce hydrogen bonding interactions and create LMWGs. For example, these moieties are used to create linear alkyl compounds spaced by multiple amide or urea groups to provide self-assembly via hydrogen bonding interaction (Figure 2-4). For compounds **8** and **9** the length of the alkyl spacer is varied to find the optimal length for gelation. In the gemini LMOG **8** two L-lysine derivatives are linked via an alkyl spacer and it was found that its gelation efficiency decreased with increasing spacer length due to increasing solvophilicity.[52] Also, the gelation properties of the linear bisurea compound **9** depend on the nature of the spacer.[53,54] When a sterically more demanding group is used as spaced compared to an alkyl group, *e.g.* an azobenzene group, the gelation strength in various solvents was reduced.

In gelators **8** and **9** there is considerable flexibility in the spacer region which can lead to differences in directionality of the hydrogen bonding interactions of the two moieties or even to the formation of intermolecular hydrogen bonds. Therefore, more rigid scaffolds were studied as well in which the direction of the hydrogen bonding interaction is guided. Examples of these types of gelators are the cyclohexyl based bisamide **10** and bisurea **11** gelators.[21,54] In these compounds the hydrogen bonding groups are trans positioned at the cyclohexane ring and adopt an antiparallel conformation. The effect of the stereochemistry on the hydrogen bonding units does not have any effect on their gelation behaviour as the gels formed by the *R,R*- or the *S,S*-enantiomer have the same physical properties, except for the helicity of the fiber. The direction of the hydrogen bonding interactions is of importance as the *cis*-isomers of these gelators do not display gelation behaviour, most probably, due to the formation of intramolecular hydrogen bonds. These compounds are potent gelators when sufficiently long alkyl tails ($>C_9$) are present and low cgc's are found in solvents of varying polarity. By changing the cyclohexyl framework to a phenyl scaffold **12** the gelation properties deteriorate as the gels formed by these compounds crystallise over time.

The rigid cyclohexane core of these gelators is such an effective scaffold that functionalisation of the alkyl chain ends does not influence its gelation properties. When amine functionalities are positioned at the end of the alkyl tail, it makes the compounds water soluble and gelation of water can be performed.[55] By positioning of acryl groups at the end of the alkyl tails the gel fiber can be stabilised by polymerisation upon irradiation[56] and also the so-called "click" chemistry with copper ions, diazides and acetylenes can be performed on these compounds by positioning of acetylene groups at the end of the alkyl tail.[57]

The number of hydrogen bonding moieties attached to a cyclohexane ring can be increased further. This is shown in the class of so-called ”tripodal” gelators where 1,3,5-substituted cyclohexane rings are used as scaffold to attach hydrogen bonding moieties. The advantage of these systems is the c_3-symmetry of the central ring which is of use in self-assembly. The tripodal gelator **13** based on the aggregative properties of amide groups together with van der Waals interactions provided by long alkyl tails is an excellent gelator for various solvents.[58]

In order to introduce additional stabilisation of the gel fiber by π-π interactions the phenyl based tripodal gelator **14** was developed. However, this compound is a weaker gelator, most probably due to the lack of the stereochemistry of the ring.[59] Compound **15** is similar to **14**, but uses urea groups for self-assembly. It does show gelation behaviour and forms helical, elongated columnar aggregates.[60]

Furthermore, another method to create new gelator systems is a combination of two successful structures of gelling agents in the same molecule and these posses more functionality compared to the individual gelators. The use of multiple components to achieve gelation is also possible.

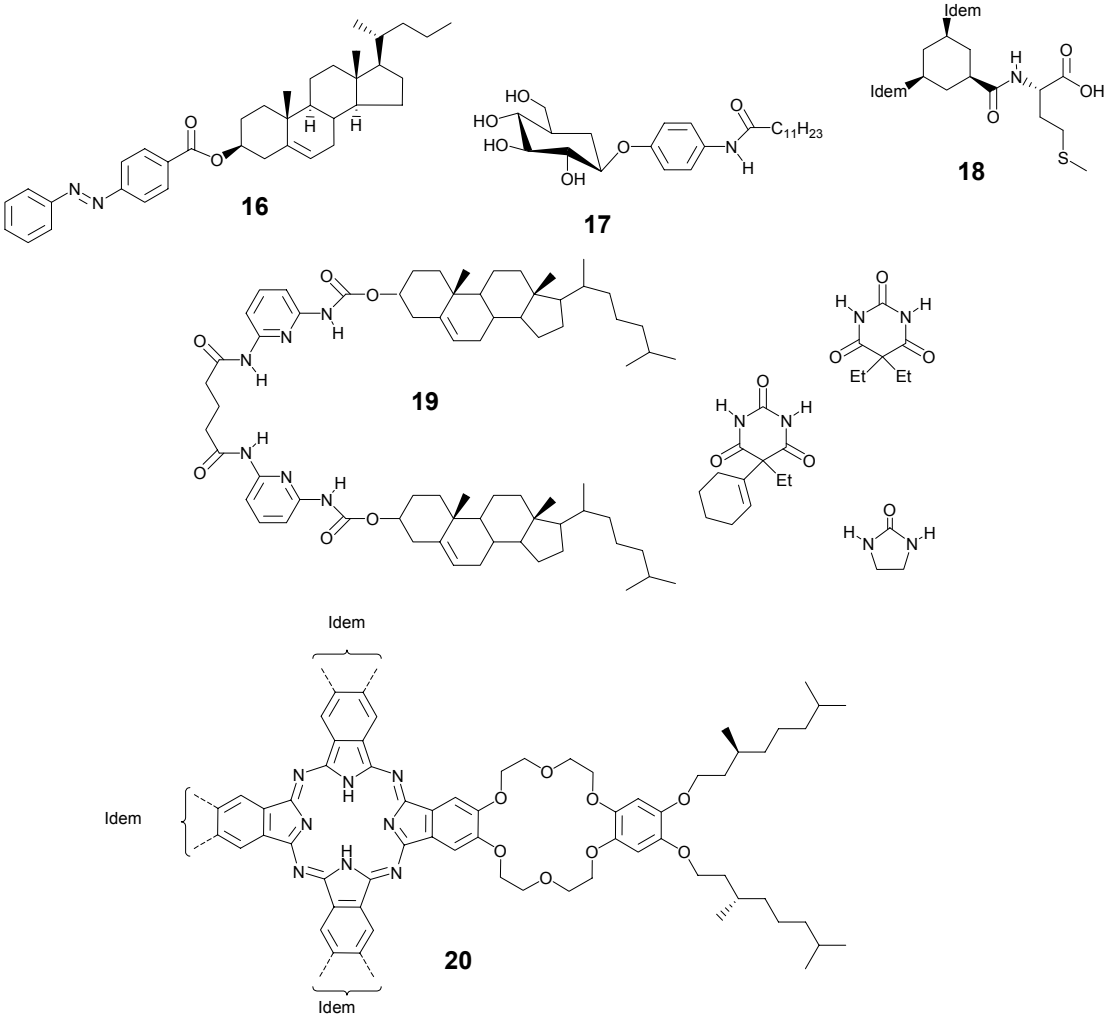


Figure 2-5. Examples of new gelators which consist of different functional groups.

The so-called Aromatic Linker Steroid (ALS)-class of gelators consists of steroid based gelators which have been linked to aromatic systems (Figure 2-5).[61,62] The ALS-gelators are more versatile in gelation compared to their individual components in terms of solvent scope. A well known example of a successful ALS-gelator is **16**, developed in the group of Shinkai, which can transcribe the chirality of its gel fiber to silica via calcination.[63] Additionally, it can switch the chirality of its gel fiber via *cis* – *trans* isomerisation of the azobenzene part on the gelator.

Based on the success of DBS, many different sugars have been derivatised in order to create new gelating agents. In this respect **17** is an example in which another class of gelling agents, aliphatic amides, is combined with sugars to create a successful gelator.[64] The stereochemistry of the sugar moiety is important and replacement with a different sugar reduces its gelation properties.

The tripodal gelators are a successful class of gelator with different types of peptides. By substituting the rigid cyclohexane framework of the tripodal gelator with different types of peptides effective hydrogelators have been developed.[65] Compound **18** is an excellent example of these types of gelators and has as additional property that its gelation behaviour in water can be tuned via the free acid groups.

In the field of multiple components the use of host-guest interaction was explored in the group of Shinkai to create new gelling agents.[66] A host molecule which possesses a 2,6-(dimethylamino)pyridine moiety linked to two cholesterol groups **19** binds via hydrogen bonding interactions to a complementary barbital or ethyleneurea guest in a 1:1 ratio. In absent of the guest, the host is soluble, however, upon complexation with the guest the hydrogen bonds formed align the cholesterol moieties in the host and via van der Waals interactions a gel fiber is formed.

Compound **20** is a large phthalocyanide-based LMOG. These types of structures are known for their aggregation behaviour[67] and in **20** four crown ethers together with long alkyl chains are attached to support the self-assembly. Upon aggregation this compound forms left-handed coiled-coil aggregates, where the helicity is directed by the chiral alkyl tails. However, by addition of KCl the crown ethers bind to the K^+ ions and the helicity of the aggregate is destroyed. In uncomplexed **20** the aggregation is driven by π-π stacking interactions and van der Waals interactions creating a chiral rod. In the complexed species **20** the main driving forces are electrostatic interactions and the compound forms non-helical rods.[68]

2.5 Functional Gels

One of the more challenging goals in chemistry is to achieve control over the structure of macromolecules.[69] The ability of LMOG to self-assemble via non-covalent interactions in structured arrays and the thermoreversibility of this process make these systems excellent candidates to reach this and to be used in functional materials.[70] A selection of LMOG will be discussed in which their unique properties were used to create functional materials.

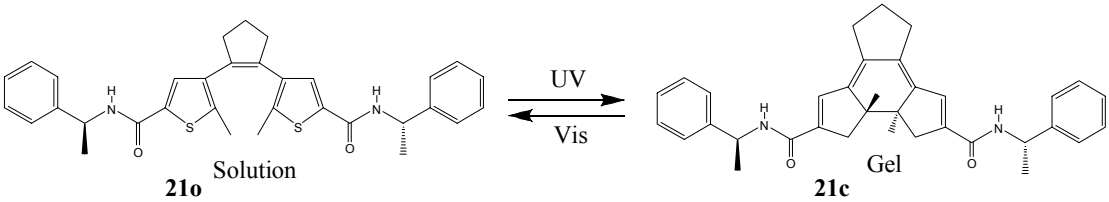


Figure 2-6. Photo-induced gelation performed by irradiation of dithienyl cyclopentane switches.

Light sensing can be performed by dithienyl cyclopentane-based compounds which switch form an open to a closed state by irradiation with UV-light. When these compounds are functionalised with amide groups, gelation can be induced by light (Figure 2-6).[71] Irradiation of a solution containing dithienyl cyclopentane switches **21** with UV-light lead to switching from the open to a closed state. Due to the increase in molecular rigidity these compounds now have a higher tendency to aggregate and a gel is formed. These compounds can be regarded as light sensors as the gelation can be reversed by irradiation with visible light. Other compounds which are capable to induce gelation upon irradiation are *e.g.* the ALS-gelator **16**[63] or derivatives of 2*H*-choromene.[72]

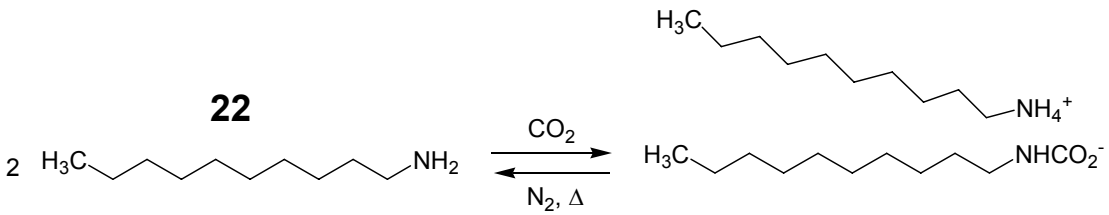
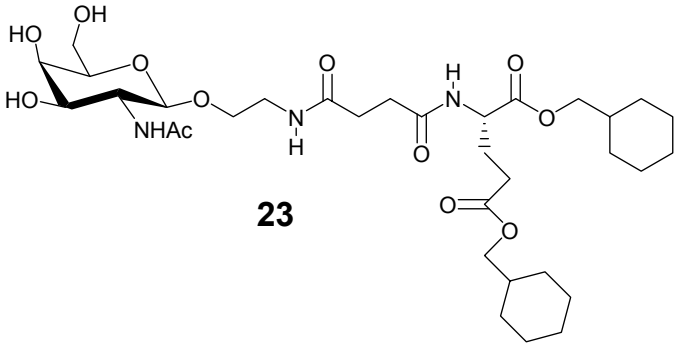


Figure 2-7. CO_2 induced gelation by primary amines.

CO_2 sensing can be performed by aliphatic primary and secondary amines. By complexation with CO_2 these compounds form ammonium salts, which are good LMOGs by themselves.[73] When a solution of primary or secondary amines, *e.g.* **22**, is exposed to CO_2, **22** is converted into the corresponding ammonium salt (Figure 2-7). As the ammonium salts have a low solubility, they aggregate and form a gel isothermally. The gel formation is completely reversible as the CO_2 can be removed

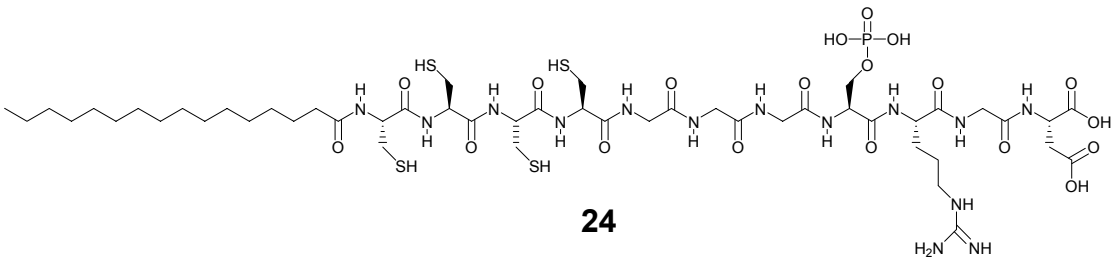
by flushing with N_2 at elevated temperatures. The behaviour of these compounds can be used in carbon dioxide sensors.



23

Figure 2-8. *N*-acylgalactosamine hydrogelator which shrinks upon heating.

Temperature-responsive gels were reported by Hamachi.[74] Unlike common gels, which dissolve at elevated temperature due to the break down of the intermolecular interactions, the gel formed by **23** shrinks upon heating (Figure 2-8). The shrinkage of the gel at 72 °C is the result of expulsion of water out of the gel matrix and due to the extremely strong H-bonding the overall 3D-network in the gel remains intact. Upon cooling to room temperature water is taken up by the gel matrix, the gel swells and it regains its original volume.



24

Figure 2-9. Chemical structure of a pH responsive amphiphilic oligopeptide.

Only pH responsive hydrogelators are known. An example of such a system is the pH-responsive hydrogelation by the amphiphilic oligopeptide **24** (Figure 2-9).[75] At pH 8 this compound is highly soluble in water (> 50 mg mL^{-1}), however, upon acidification of the solution to a pH of 4 aggregation occurs. The compound becomes insoluble and forms a birefringent gel. When the pH of the system is brought back to neutral with KOH, the gel disassembles and a solution is regained. This process can be repeated many times. Other systems that display this type of behaviour are often based on peptides containing either free acid or amine groups and include, peptide-based tripodal gelators, *e.g.* **18**,[65] a *β*-hairpin peptide,[76] or various oligopeptides.[77]

Other useful functions of gels include, the gelation of liquid crystalline materials,[78] electrolytes[79] and entrapment of drug particles for slow release of medicines which is particular useful in pharmaceutical applications.[80]

2.6 Conclusions

Over the years many different systems have been found or designed which show gelling behaviour, some of which are efficient gelators whereas others are not. Insight into the properties of these gels is gained by the use of known techniques, *e.g.* rheology, NMR and FTIR spectroscopy or by the development of new techniques to study the organisation in the gel fiber. This has been demonstrated by the use of SAXS to examine the dimensions of gel fiber in their native state. However, the exact interactions and conformation of gelators in the gel state is often not known due to the inherent lack of gelators which crystallise, making then unsuitable for single crystal X-ray diffraction. Therefore, powder X-ray diffraction may be used in the future to predict from the scatter profile the crystal structure as used in small molecule pharmacophores already with success. Research on gelator system nowadays has almost reached the point at which compounds can be designed rationally, based on structural features found in known gelators. However, the exact mechanism behind gel formation and the effects of the different intermolecular interactions, solvents, etc. is still understood poorly. This means that the size of the gel fiber and the mechanical properties are still difficult to predict.
This thesis will focus only a small number of structurally similar gelators in order to distinguish between the contribution of different intermolecular interactions that lead to gel fiber formation and to examine the role of the solvent on gel fiber stability. Ultimately, we hope to be able to establish design rules for new gelators with predictable properties and functions.

2.7 References

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